Guadecitabine sodium

Cat. No.: HY-15229

CAS No.: 929904-85-8

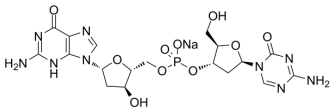
Molecular Formula: $C_{18}H_{23}N_9NaO_{10}P$

Molecular Weight: 579.39

Target: DNA Methyltransferase

Pathway: Epigenetics

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 50 mg/mL (86.30 mM; Need ultrasonic and warming)
DMSO : 50 mg/mL (86.30 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7260 mL	8.6298 mL	17.2595 mL
5 mM	0.3452 mL	1.7260 mL	3.4519 mL
10 mM	0.1726 mL	0.8630 mL	1.7260 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 33.33 mg/mL (57.53 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Guadecitabine sodium (SGI-110 sodium) is a second-generation DNA methyltransferases (DNMT) inhibitor for research of acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS)[1].

IC_{50} & Target

DNMT1

In Vitro

After HCT116 colorectal carcinoma cells are treated for 6 days, a dose-dependent increase in p16expression is observed with

	Guadecitabine sodium (SGI-110 sodium). In addition, T24 and HCT116 cells treated with Guadecitabine sodium or 5-aza-CdR for 3 days show a dose-dependent increase in the level of p16 protein, showing the competence of Guadecitabine sodium to inhibit DNA methylation and induce p16 at both mRNA and protein levels as well as 5-aza-CdR. Thus, Guadecitabine sodium is able to inhibit DNA methylation at 5′-region and induce the expression of the p16 gene in T24 and HCT116 cells at concentrations comparable to 5-aza-CdR, and the induction of p16 expression by both agents correlates with the demethylation at the 5′-end region of the gene in both cell lines. Guadecitabine sodium is slightly less toxic than 5-aza-CdR at the doses tested up to 1 μM concentration but displaying similar toxicity at 10 μM concentration[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Guadecitabine sodium (SGI-110 sodium) at 10mg/kg is an effective dose at reducing DNA methylation and retarding tumor growth, and caused roughly the same level of toxicity as 5-Aza-CdR. Guadecitabine sodium is effective in vivo at reactivating the expression of the p16 gene, which is heavily methylated in the parent EJ6 cells. Guadecitabine sodium is effective in reducing the level of DNA methylation in vivo at the p16 promoter region. Guadecitabine sodium is better tolerated than 5-Aza-CdR in vivo, suggesting that it can be an attractive alternative for potential clinical use[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	T24 cells are plated at a low density (100 per 60-mm dish) and treated with varying concentrations of 5-aza-CdR and S-110 (0.1, 0.2, 10 μM. Colonies are allowed to form for 10 to 14 days, fixed with methanol, and stained with 10% Giemsa. The number of colonies from an untreated control plate is used to calculate the plating efficiency in percent at each concentration. Triplicate dishes are used, and error bars are represented by 1 SD of the mean[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mouse: Athymic nu/nu mice are inoculated subcutaneously in the right hind flank with 10^7 EJ6 bladder cancer cells. After tumors reach 0.5 cm in diameter, animals are stratified into three groups with eight animals per group to begin treatments. Doses and dosing schedules are designed so that each group received molar equivalents of either S-110 or 5-Aza-CdR. The agents are administered SQ once weekly at a dose of 12.2 mg/kg for S-110 and 5.0 mg/kg for 5-Aza-CdR for three weeks. The study includes an appropriate PBS control group. Tumor sizes by caliper and body weight measurements are taken twice weekly to monitor tumor growth inhibition and tolerability[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cell. 2022 Sep 29;S1097-2765(22)00896-6.
- Cancer Res. 2020 Jul 15;80(14):3046-3056.
- J Exp Clin Cancer Res. 2023 Mar 18;42(1):67.
- Neoplasia. 2020 May 25;22(7):274-282.
- Research Square Print. January 3rd, 2023.

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REFERENCES

[1]. Yoo CB, et al. Delivery of 5-aza-2'-deoxycytidine to cells using oligodeoxynucleotides. Cancer Res. 2007 Jul 1;67(13):6400-8.

[2]. Chuang JC, et al. S-110, a 5-Aza-2'-deoxycytidine-containing dinucleotide, is an effective DNA methylation inhibitor in vivo and can reduce tumor growth. Mol Cancer

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